CALIFORNIA INSTITUTE FOR REGENERATIVE MEDICINE

California Institute for Regenerative Medicine (CIRM)
Scientific Strategic Planning
Strategic Planning Advisory Committee Meeting
July 10, 2006

The fourth meeting of the Strategic Planning Advisory Committee (SPAC) included a progress report on interviews and meetings conducted to date as well as a discussion centered on two topics: technologies for stem cell research and training. In the course of this meeting, a number of ideas arose which are summarized below. This summary is not intended to be comprehensive with respect to reporting these ideas; inclusion in this summary does not imply any commitment or endorsement by the CIRM.

A. Progress Report

1. Update on CIRM Training Grant Program

a. Sixteen sites have been awarded training grants. A meeting of the program directors (or their delegates) was held at CIRM on June 20 to meet each other, provide an update of trainee recruitment and highlight unique aspects of each of their programs.

b. Over half of the trainees have been recruited and the applicant quality is very high; the institutions are getting first rate people into the training program.

c. The training program encompasses research activities spanning a wide variety of disciplines, including computational chemistry, engineering as well as the expected cell/molecular biology. Several social scientists are also involved in the program. The proposed annual meeting for trainees should provide an excellent opportunity for the trainees to meet and to talk to people inside and beyond their fields.

d. The discussion highlighted a general need for courses related to the derivation and handling of stem cell lines.

2. Update on Interviews

a. To date, 35 interviews have been completed and 17 more are currently scheduled.

3. Update on Other Meetings

a. SPAC members and meeting participants were reminded of the upcoming scientific conference scheduled for July 13 on the topic of "The Scientific Challenge: Basic Science to the Clinic" and updated on the participating speakers. The Grants Review

Working Group has been invited to the meeting, which will be held at the Gladstone Institutes.

b. SPAC members and meeting participants were also invited to a strategic planning conference on July 25 on the topic of "Industry and Stem Cells in California: Fostering R&D".

c. Two focus groups will be held and will not be public meetings. One is a patient advocate focus group and the other is a diversity focus group.

d. There will be an ICOC meeting in early August where we will continue to discuss the mission, values, and long-term objectives.

B. Discussion Topics

1. Technologies for Stem Cell Research

a. Before the discussion on what technologies are needed for stem cell research and CIRM's role with regards to these new technologies was begun, Dr. Hall provided a brief overview of some of those technological needs:

   i. Imaging with respect to tracking stem cell delivery and activity is particularly difficult in humans due to the low penetrating power of current imaging modalities. Imaging in mice, as they are much smaller, is much easier.

   ii. With respect to cell separation, while there are multiple methods for cell separation, the consensus seems to be that there is a dearth of reagents specific for identifying classes of cells and their derivatives.

   iii. Nanotechnology may have important applications to stem cells therapies, specifically with respect to scaffolding and extracellular matrices, which may be critical to the delivery and localization of stem cells.

b. A suggestion was made that one area missing from the discussion of relevant technologies is in the area of global genomic analysis with respect to stem cells and stem cell differentiation.

   i. For example, a whole genome analysis of the binding of relevant transcription factors (e.g. Oct4) could be performed with embryonic stem cells and with various differentiated cell derivatives. This is the type of resource intensive large scale analysis that CIRM would be in a position to facilitate and fund.

   ii. Affymetrix (a California based company) has particular strengths in whole genome analysis technologies including the mapping of transcription factor binding sites. Dr. Tom Gingares, VP of Biological Sciences at Affymetrix and his colleagues have developed and published on microarray technologies for unbiased, high-throughput DNA transcription factor binding site mapping as well as methylation profiling of large genomic regions.

   iii. These kinds of analyses could lead to a deeper understanding of stem cell development and differentiation, which could be a significant contribution to progress in the field.

c. A suggestion was made that CIRM could also look at supporting attempts to advance techniques for micromanipulation and to advance the robotics of cell manipulation, particularly to allow robotic microinjection of stem cells.

d. Technology development for biomaterials for tissues engineering with stem cells or derivatives will require collaboration with bioengineers.
   i. There is interest among the engineering community in making ties between the fields of life sciences and biomaterials; applying biological materials to cell growth could help advance the field.
   ii. Progress in biomaterials development or in other areas of technology development may be facilitated if scientists had access to stem cells or their derivatives. This need could be provided by a core facility for growing cells.

e. The role of the CIRM in supporting the development of antibodies related to stem cell research was discussed.
   i. Antibodies are still an unmet need in the stem cell community.
   ii. It may be useful to develop a comprehensive panel of antibody reagents that recognize a variety of markers on stem cells and their derivatives. Especially in the area of cancer stem cells, these could have particular utility not only in research but also potentially as diagnostics and or therapeutics.
   iii. There is also a need for good antibodies against all transcription factors (which would only work on cell lysates) as well as for proteins on the cell surface; CIRM could consider supporting an effort for the development and characterization of monoclonal antibodies that could be made available through a core reagent facility.

f. Additional technology needs were also discussed.
   i. There is limited technology with respect to high throughput cell assay procedures. Industry can "churn out" any number of compounds; what is missing is a validated biological system on which to assay them.

g. Core service centers that make technologies widely available, such as the four fluorescence activated cell sorter (FACS) centers at Harvard, have proven to be a tremendous boon to research at the university.
   i. An effective FACS core facility with 2-3 high speed sorters and associated analytical instruments requires a Masters level (or comparable) scientist to run it and 2-3 supporting technicians. Depending on staffing, such a facility could, in theory, operate 24 hours per day. The cost to set up such a facility was estimated at $2.5MM (presumably for equipment purchases) excluding staff salaries.
   ii. There is a certain level of expertise required of technicians in such a core and the learning curve is steep, but the technology is central to what stem cell biologists do.

iii. Capital costs for such a core facility could be funded through a variety of mechanisms; ongoing operational costs could be funded, at least partially, on a 'recharge' basis.

iv. Increasingly, there is recognition of a need for complementary technology to fluorescence activated cell sorters; cell sorters that could sort hundreds of cells rather than the millions required for FACS use. Microscale sorters, including microfluidic sorters, may be particularly useful for stem cell isolation and single cell analysis. Highly parallel microfluidic based cell sorters would allow for a dramatic scale up of throughput and scale down of the related pressures and could serve the goals of the stem cell community.

h. The mechanisms to push technology tools forward were also discussed.

i. Multi-disciplinary workshops that bring together persons of disparate expertise (e.g. doctors, basic scientists and engineers) to brainstorm technology solutions to biological/biomedical problems could be one way to address new technology development.

ii. More dynamic interaction with companies and relationships with commercial players may also be needed to facilitate technology development.

iii. The Defense Advanced Research Projects Agency (DARPA) model was cited as an exemplary model for how to encourage technology development.

2. Training

a. CIRM envisages training not only scientists and clinicians but also the skilled technical people that will be performing the research. Laboratory work, including the culture and maintenance of stem cells is labor intensive and requires technical expertise. There are a number of relevant training programs in development throughout the state.

i. Pasadena Community College was cited as an example of an organization that has a training program in the culture of stem cells.

ii. CIRM has participated in an initial meeting with California State University (CSU) representatives to see how CIRM and CSU might work together. Under the auspices of the Chancellor's office, CSU is putting together a white paper on how the CSU and California community college system can train the technical people and candidates for graduate school that will contribute to a vital stem cell and biotechnology workforce.

1. CSU trains many of the BA/BSs who carry out scientific research. CSU is also the largest feeder of students into the UC basic science PhD programs

iii. A representative of the Bay Area Funding Collaborative of the SF Foundation indicated an interest in working with CIRM to explore job training in the stem cell/biotechnology related activities for a broad based group of people.

iv. These types of programs highlight the opportunities CIRM may wish to pursue that not only address a need for skilled technical people at all levels but also could

provide an opportunity for CIRM to broaden its reach to the diverse California population.

b. CIRM would like to encourage physician scientists to conduct stem cell related research. The biggest problem for physician scientists and clinical faculty who are just starting out is that the funding for research at their home institutions is limited, so they must support themselves through clinical obligations, which makes it difficult to give them protected time for research.
   i. The question of sophisticated training in clinical research was briefly discussed; CIRM might consider looking at ways to stimulate such training.

c. A question was raised about whether there has been a systematic study of the types of training, their geographic distribution, etc. that would give the most return to the state of California. One way to measure return on investment is to look at the people doing work in the field who were not doing that work before. CIRM could consider a RFA to address this question.

d. Training in grantsmanship was discussed, but there was some debate about whether or not such training falls outside of CIRM's purview.

C. Public and Additional Comment

1. There was a discussion regarding whether CIRM should provide funding to small companies, knowing some will create "homeruns", and whether this fell under creating infrastructure.
   a. A participant observed that the trend in the venture capital (VC) world is much different from what was seen in the 90s when longer lead times [prior to VC exit] were allowed; VCs are now looking for shorter timelines so basic science research funding is unlikely to come from VCs. CIRM therefore has a potentially critical role in helping to fund small companies. Nevertheless, even small companies would not take grants if CIRM’s intellectual property (IP) policy was not compatible with their ability to compete. CIRM might therefore wish to mirror the Small Business Innovation Research (SBIR) program.
   b. CIRM will allow companies to compete [for funding] in as many areas as possible, and in areas where companies can do things better, they should be funded.
   c. A participant stressed that having an IP policy that will not discourage companies or create a disincentive to innovate will be critical. This is being addressed by the IP Task Force.